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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/045,292	10/18/2001	Lieven Stuyver	09797.0004-00	4833

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EXAMINER	
MCINTOSH III, TRAVISS C	

ART UNIT	PAPER NUMBER
1623	

MAIL DATE	DELIVERY MODE
07/07/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/045,292	STUYVER ET AL.	
	Examiner	Art Unit	
	TRAVISS C. MCINTOSH III	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 March 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,35,36,39,44,50,51,59,60,66 and 67* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,35,36,39,44,50,51,59,60,66 and 67* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/31/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The Amendment filed 3/10/2009 has been received, entered into the record, and carefully considered. The following information provided in the amendment affects the instant application by:

Claims 1-2, 44, 59-60 and 66 have been amended.

Claims 3-34, 37-38, 40-43, 45-49, 52-58, 61-65, and 68-70 stand as being canceled.

Remarks drawn to rejections of Office Action mailed 9/11/2008 include:

Claim objections: which have been overcome by applicant's amendments and have been withdrawn.

112 1st paragraph rejections: which have been overcome by applicant's amendments and have been withdrawn.

112 2nd paragraph rejections: which have been overcome by applicant's amendments and have been withdrawn.

102(b) rejection: which has been overcome by applicant's amendments and has been withdrawn.

103(a) rejection: which has been maintained for reasons of record.

An action on the merits of claims 1-2, 35-36, 39, 44, 50, 51, 59, 60, 66, and 67 is contained herein below. The text of those sections of Title 35, US Code which are not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 2, 35, 36, 39-41, 44, 50-51, 55, 59-60, 66, and 67 are rejected under 35 U.S.C. 103(a) as being unpatentable over Loeb et al. in view of Filippini et al. (Arch Virol

(2000), 937-944 - of record) LaColla et al. (6,812,219 – of record) and Shealy et al. (J. Med Chem., 1986 (29) 1720-25 – of record from IDS filed 4/30/08).

The claims of the instant application are drawn to methods of treating various viral infections, such as from Flaviviridae (specifically HCV), Orthomyxoviridae, or Paramyxoviridae infections using various nucleosides.

Loeb et al. teaches to treat various viral infections with modified nucleosides which induce a mutation in the virus wherein the increase in mutation rate results in a reduced viability of progeny generations of the virus. Various modified nucleosides administered include 5-hydroxycytidine and N4-aminocytidine, which are encompassed by the claims as set forth supra. Loeb et al. disclose methods of treating various viral infections, including HCV, flavivirus, influenza virus, measles, mumps, and RSV (see page 7, lines 23-35) with various modified nucleosides, such as with N4-aminocytidine, 5-hydroxycytidine (page 26, 1st full paragraph) and 5-hydroxyuridine (page 9, line 21). What they do not teach is the additional various claimed compounds for treating the viral diseases.

Filippini teaches methods of treating HCV and HIV patients with various nucleosides such as zalcitibine, which is a 2',3'-dideoxynucleoside.

LaColla et al. disclose a multitude of modified nucleosides, including 2',3'-dideoxy nucleosides, for the treatment of flavivirus, and HCV infections. See column 143, line 18.

Shealy et al. teach that various 5-halocytosine compounds have analogous properties in inhibiting viral replication.

It would have been obvious to one of ordinary skill in the art to modify the various nucleosides of the prior art to treat various viral infections with these references before them.

Obviousness based on similarity of structure and function entails motivation to make claimed compound in the expectation that compounds similar in structure will have similar properties. Where the prior art compounds essentially bracket the claimed compounds and are known to be effective as well known pesticides, for example, one of ordinary skill in the art would be motivated to make the claimed compounds in searching for new pesticides. See ***In re Payne, 606 F.2d 303, 203 USPQ 245, 254-55 (CCPA 1979).*** Moreover, it would be obvious to treat other members of Flaviviridae, Orthomyxoviridae, or Paramyxoviridae viral infections with the same drugs, as Loeb teaches that overlapping modified nucleosides can be used to treat all of the above classes of viral infections. As such, applicant's provisos are not seen to render patentable the claims, as the compounds delimited would still be seen to be obvious to treat other flavivirus infections, for example, or treat the flu. Moreover, modifying zalcitibine with a 5-fluoro group on the base would also be obvious, as various 5-halogen cytidine compounds are taught to be effective in Loeb et al. (see cytidine compounds on page 26) and Shealy et al. The art teaches various divergent nucleoside derivatives are effective in treating the same groups of viral infections claimed in the instant application. As such, absent unexpected results, the methods of treating obvious viruses with obvious compounds is seen to be obvious in view of the references.

Applicant's arguments filed 3/10/2009 have been considered but are not persuasive. Applicants argue that Loeb does not teach the additional various claimed compounds for treating viral diseases, thus cannot render obvious the instant claims. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375

(Fed. Cir. 1986). Applicants also state that no rationale is set forth why a skilled artisan would have modified the naturally occurring ribonucleosides of Loeb. The examiner notes one would have modified them in searching for other drugs to treat viral diseases. The support for the modifications comes from the other references, which have modifications as are encompassed by applicants extremely broad group of compounds, which have various art known compounds delimited. Applicants argue that it still remains necessary in cases involving new chemical compounds to identify a reason a chemist would modify the compounds, however, the examiner does not believe this applies here, as these are not new compounds being claimed, and no compounds are claimed in the instant application. Applicants argue that the examiner has provided general statements asserting overlap at various positions of art recognized compounds, however, the examiner believes applicants have not clearly shown what their invention is, and with such a broad disclosure with no showing of criticality of any specific novelty, the examiner believes a general teaching is enough to render obvious the instant claims. The examiner is unable to determine what the actual invention is, as applicants normally have a special feature which provides efficacy not known in the art, for example, compounds which may require a 2'-methyl group, or a 4'-cyano group, and the compounds of the instant application are not seen to have anything novel in all of the compounds which are seen to provide the beneficial therapeutic efficacy. While Loeb is drawn to modifications of ribonucleosides, this does not negate the fact that Filippini teaches compounds which are deoxyribose compounds (stavudine and zalcitibine for example) LaColla teaches deoxy nucleosides, and Shealy teach analogous properties of various 5-halocytosine compounds. Applicants arguments and declaration filed regarding the different mechanism of action for Loeb as compared too the instant compounds is also not found

to be convincing. Because the instant compounds work via a different mechanism of action does not mean the methods of treating the same diseases are not rendered obvious by the art. Applicants arguing that changes in the structure of the sugar or base may have unpredictable effects is akin to stating that the untested compounds embraced by the instant application, which number in the thousands, are not enabled. The art teaches the same class of drugs, and also the same various modifications embraced by the instant compounds, to be used to treat the same viral diseases. Applicants have not shown any specific portion of the compounds which provides the unexpected activity as asserted, and the examiner notes that a broad and generic teaching is met by the same.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to TRAVISS C. MCINTOSH III whose telephone number is (571)272-0657. The examiner can normally be reached on M-F 9:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia A. Jiang can be reached on 571-272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Traviss C McIntosh III/
Primary Examiner, Art Unit 1623
June 22, 2009